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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Kevy et al.	Confirmation No.:	1436
Serial No.:	10/765,694	Group Art Unit:	1657
Filed:	January 27, 2004	Examiner:	Laura J. Schuberg
Title:	AUTOLOGOUS COAGULANT PRODUCED FROM ANTICOAGULATED WHOLE BLOOD		

To: Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Supplemental Response to Office Action

Dear Sir:

This paper is submitted in support of Applicants' timely filed response of March 11, 2008 to the Office Action mailed on September 11, 2007, in connection with the above-identified U.S. patent application.

Enclosed herewith is a copy of a brochure describing the "Thrombin Processing Device (TPD™) (marketed by ThermoGenesis Corp.), which Applicants believe is the subject matter of U.S. patent 6,472,162 (referred to hereinafter as the '162 patent) assigned to ThermoGenesis Corp. Note that the brochure bears a copyright notice dated 2002-2004.

Page 1 of the brochure shows a picture of the device and states:

> ***"The Thrombin Processing Device (TPD™) produces active human thrombin from approximately 11 ml of plasma in 25 minutes*"***

Under "*Enhanced Product Safety*," the brochure indicates that the device utilizes autologous or allogeneic ***plasma***. On page 2, the steps for using the device to produce thrombin include: 1) add thrombin reagent; 2) Add ***plasma***; and 3) Harvest active thrombin after processing.

The brochure contains no textual or photographic information from which one of skill in the art would conclude that the device was intended for use with whole blood.

The brochure is presented in support of Applicants' contention that, at the time of the invention by Applicants, isolation of plasma from whole blood prior to further processing was standard in the art for preparing fibrin sealant materials from blood. In support of this position, a Declaration Under 37 CFR §1.132 was submitted (response filed June 14, 2007) to establish that, at the time the present application was filed, one of skill in the art would have recognized that precipitation of an anticoagulated whole blood preparation would result in a preparation containing significant levels of cell debris and cellular proteins not present in a similarly processed plasma preparation from which the cells have been removed (Declaration of Sherwin V. Kevy, M.D. June 13, 2007, paragraph 12) and that prior to 2006, no report of a method using whole blood without the plasma isolation step had been made; the standard of practice in the art for production of thrombin from whole blood included a plasma isolation step for the removal of cells/cell debris prior to precipitation of protein components, leaving soluble thrombin in the supernatant.

Additionally, Applicants submitted in support of the state of the art an article by ThermoGenesis ('162 patent) scientists, Kumar and Chapman, (JECT 39:18-23, 2007) first reported generating autologous human thrombin from whole blood as the starting material (abstract). The Kumar reference represents the first disclosure of that which Applicants had already invented.

The abstract of the Kumar article states:

> "Thrombin-based clotting agents currently used for topical hemostasis with absorbable sponges, fibrin sealants, and platelet gels *are primarily derived from bovine or pooled human plasma sources*...The goal of our research was to develop a rapid, reliable, and simple to perform process to generate autologous human thrombin in the intra-operative setting, *from patient whole blood as the starting source material*." [emphasis added]

"In this study, we have developed a reliable technique to generate autologous human thrombin in the intra-operative setting *from whole blood instead of plasma as the starting source material* within a 30-minute period." [emphasis added]

Applicants urge, therefore, that the Declaration of Dr. Kevy, and the Kumar reference, already of record in this case, and the instant ThermoGenesis brochure submitted herewith, when taken together establish that, at the time of the disclosure by Coelho et al. of a method for extracting thrombin from blood, the skilled artisan would not have thought it feasible let alone advantageous to precipitate plasma proteins without first removing blood cells, i.e. isolating the plasma fraction.

It is respectfully submitted that the above-identified application is now in condition for allowance and favorable reconsideration and prompt allowance of these claims are respectfully requested. Should the Examiner believe that anything further is desirable in order to place the application in better condition for allowance, the Examiner is invited to contact Applicants' undersigned attorney at the telephone number listed below.

Respectfully submitted,

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Dated: May 2, 2008

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